IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. Ser. No.: 10/648,089 Docket No.: 09820.286

Filing Date: August 26, 2003 Group Art Unit: 1654

Applicant(s): Gellman et al. Examiner: Kosar

Title: HETEROGENEOUS FOLDAMERS CONTAINING α-, β-, AND/OR γ-AMINO ACIDS

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APPELLANTS' REPLY BRIEF

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I certify that this paper is being electronically submitted to the U.S. Patent and Trademark Office via the PAIR (Patent Application Information Retrieval) system on August 11, 2009

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ARGUMENT

Appellants respectfully submit that the Office has improperly discounted the Rule 132 Declaration of Dr. Samuel Gellman and the nexus between the data presented in the Declaration and the original disclosure of the application as filed. Applicants further submit that the Office has misconstrued Dr. Gellman's citation to the Petros et al. paper in his Declaration. The Declaration articulates the exact patentable utility set forth in the application as filed, using a compound within the scope of the claims, and that same patentable utility was also well known in the art at the time the application was filed. (See §§ I and IV of Appellants' Brief, starting at pages 10 and 19, respectively.) Appellants submit that the Office is improperly discounting the data presented in Dr. Gellman's Declaration and its nexus with the information contained in the application as filed.

Specifically, in the passage spanning 9 and 10 of the Examiner's Answer, the Office has taken the position that "Dr. Gellman's declaration *would have possibly* provided enablement **had the instant specification provided explicit direction to the selection of Bcl-x_L-BH3 interaction and the specific probe that was used in the declaration**." (Emphasis in original.) Appellants respectfully note that the probe described by Dr. Gellman in his Declaration **is literally encompassed** by the present claims, a

fact noted at paragraphs 12 and 13 of Dr. Gellman's Declaration itself. Appellants are not required to point to any one species within a claimed genus as being any "better" than any other. In short, compounds within a claimed genus need not be equally effective. (See, for example, *In re Gardner*, 177 USPQ 336 (CCPA 1973). Thus, Applicants have no duty to point to any specific compound within the genus as having the recited utility because all of them have the recited utility to one degree or another. The Office's insistence that Appellants call out one or more individual species within their specification as filed is reversible error.

Regarding the Bcl-x_L-BH3 example presented in Dr. Gellman's Declaration, it is a straightforward illustration **of the exact utility asserted** in the application as filed. See pages 11 and 12 of Appellants' Brief. Appellants note that the Examiner's Answer at page 10 turns the issue on its head. Appellants have asserted that the utility presented in the application is well known. Dr. Gellman's Declaration was submitted as evidence to support that well known utility. Dr. Gellman could have chosen any number of protein-protein interactions to illustrate the patentable utility of presently claimed compounds; he chose the Bcl-x_L-BH3 interaction. Using the Examiner's standard, had Dr. Gellman illustrated the same well known utility with 50 different protein systems, the Office still would be entitled to

make this rejection. Appellants note, however, that where a well known utility is present, they do not need to describe that utility in great detail in the application as filed. See Appellants' Brief at page 13, citing to MPEP §2107.01(II). Appellants again note that the utility demonstrated in Dr. Gellman's Declaration is the exact same utility articulated in the application as filed.

Based on this improper standard, the Office discounts the probative value of Dr. Gellman's Declaration and cites to *In re Fisher*, 76 USPQ2d 1225, for support. Appellants submit that this is reversible error because the facts of *In re Fisher* cannot be extended to the facts of the present case. In the *Fisher* case, the claims were directed to a series of expressed sequence tags (ESTs). (An EST is a short nucleotide sequence that represents a fragment of a piece of expressed DNA - *i.e.* a very small piece of a gene captured during the process of being transcribed into its corresponding protein.) In *Fisher*, the applicant asserted seven distinct utilities for the ESTs, but admitted on the record that the underlying genes "have no known function." *In re Fisher*, 76 USPQ2d at 1231. Fisher's cause was thus hobbled from the outset by an admission that Fisher himself deemed irrelevant, but that the Federal Circuit deemed fatal. *Id.* Moreover, the Court noted, all of Fisher's asserted uses represented merely hypothetical

possibilities, objectives which the claimed ESTs, or any EST for that matter, could possibly achieve, but none for which they have been used in the real world. Lastly, and most importantly, "Fisher disclosed a variety of asserted uses for the claimed ESTs, **but failed to present any evidence – test data, declaration, deposition testimony, or otherwise** – to support those uses." *Id.* at 1234 (emphasis added).

The same cannot be said of the compounds claimed herein because the claimed compounds have been shown to disrupt protein-protein interactions, as shown in Dr. Gellman's Rule 132 Declaration. This utility was also well known at the time the application was filed, as shown by the Seebach et al. paper discussed in Section II of Appellants' Brief (starting at page 13 of the Brief). While Seebach's comopunds (gamma-peptides) are not identical to the claimed compounds (if they were, Appellants would be facing a §102 rejection), they are related and therefore highly probative to the question of well known utility. Seebach's compounds are non-natural peptidomimetics - the same type of compound now claimed.

Appellants thus submit that the *In re Fisher* case is inapposite to the present application because Appellants have submitted quite a bit of evidence, in the form of Dr. Gellman's Declaration and contemporaneous

work by others in the field, both of which prove the patentable utility of the claimed compounds.

Lastly, at the middle of page 10 of the Examiner's Answer, the Office states that "Further, with regards to Petros, it was published after the instant application and cannot be relied upon to show the asserted utility provided in the declaration was known at the time of filing." Appellants respectfully note that they **did not** make this argument in their Brief. Appellants cited to Seebach et al. as showing a well-known utility for the claimed compounds. See Section II, starting at page 13 of Appellants' Brief. The Petros et al. paper was cited by Dr. Gellman in his Rule 132 Declaration at paragraph 10, spanning pages 5 and 6 (Petros et al. is endnote 4). Petros et al. was cited by Dr. Gellman solely as **background** information as to why the Bcl-x_L-BH3 interaction was chosen as an example to illustrate the patentable utility of the present invention. In short, as stated by Dr. Gellman, the Bcl-x_L-BH3 system was chosen simply because the system is well characterized. Dr. Gellman (a scientist, not a patent lawyer) cited to Petros et al. (dated 2004) as one paper that describes the Bcl-x_L-BH3 system. There are a host of other papers, dated prior to the filing date of the present application, that describe the Bcl-x_L protein and its interaction with BH3 and other peptides. See, for example:

- Sattler M, Liang H, Nettesheim D, Meadows RP, Harlan JE, Eberstadt M, Yoon HS, Shuker SB, Chang BS, Minn AJ, Thompson CB, and Fesik SW. (**Feb. 1997**) "Structure of Bcl-xL-Bak peptide complex: recognition between regulators of apoptosis," *Science* 275(5302):983-6.
- Kelekar, A. & Thompson, C.B. (**Aug. 1998**) "Bcl-2-family proteins: the role of the BH3 domain in apoptosis," *Trends in Cell Biology*, 8(8):324-330.
- Ricky W Johnstone (**Oct. 2002**) "Deamidation of Bcl-XL: A New Twist in a Genotoxic Murder Mystery," *Molecular Cell*, 10(4):695-697
- Haichao Zhang, Paul Nimmer, Saul H. Rosenberg, Shi-Chung Ng, Mary Joseph (**Aug. 2002**) "Development of a high-throughput fluorescence polarization assay for Bcl-xL," *Anal. Biochem.*, 307(1):70-75.
- Thomas Chittenden (**Sept. 2002**) "BH3 domains: intracellular death-ligands critical for initiating apoptosis," *Cancer Cell*, 2(3):165-166.
- Anthony Letai, Michael C. Bassik, Loren D. Walensky, Mia D. Sorcinelli, Solly Weiler, Stanley J. Korsmeyer (**Sept. 2002**) "Distinct BH3 domains either sensitize or activate mitochondrial apoptosis, serving as prototype cancer therapeutics," *Cancer Cell*, 2(3):183-192.
- Yong Shi, Jianjun Chen, Changjiang Weng, Rui Chen, Yanhua Zheng, Quan Chen, & Hong Tang (**June 2003**) "Identification of the

protein–protein contact site and interaction mode of human VDAC1 with Bcl-2 family proteins," *Biochem. & Biophys. Res. Comm.* 305(4): 989-996.

- Tan, Y. et al. (**Aug. 2000**) " BAD Ser-155 phosphorylation regulates BAD/Bcl-XL interaction and cell survival," *J. Biol. Chem.* 275(33):25865-9 (2000).

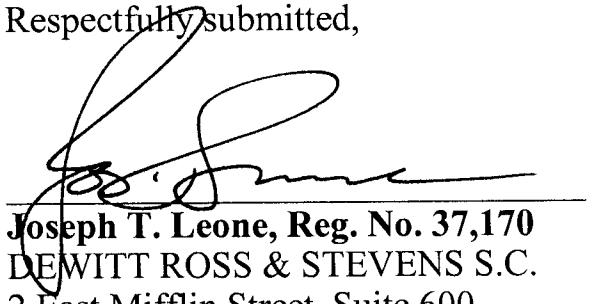
- Grant Dewson (**April 2001**) "Small, but deadly: small-molecule inhibition of Bcl-2 homologue heterodimerization," *Trends in Biochemical Sciences*, 26(4):218-219.

- Stacey E. Rutledge, Jason W. Chin, Alanna Schepartz (August 2002) "A view to a kill: ligands for Bcl-2 family proteins," *Current Opinion in Chemical Biology*, 6(4):479-485.

In short, the Petros et al. paper **was not** relied upon by Appellants to show that the utility asserted in the application as filed is well known. It was cited by Dr. Gellman solely to show the well known nature of the Bcl-x_L-BH3 system - a system that was well known prior to the filing date of the present application as evidenced by the above sampling of earlier papers describing the same system.

Appellants thus submit that the present rejections under §101 and §112 should be reversed and the application issued in due course.

Respectfully submitted,



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